Structure of a Promising New Drug for Photodynamic Therapy

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Beamline(s): **X7B**

Introduction: Photodynamic therapy (PDT) is a technique that combines light, oxygen and a sensitizer (drug) to attack cancerous and other diseased cells. Among the promising new second generation photosensitizers for PDT are benzochlorins and their derivatives, i.e., porphyrins in which one of the four pyrrole rings is reduced. Despite the intense biophysical, chemical and medicinal interest in reduced porphyrins, there are few high precision structures of the chromophores. Since these are highly substituted porphyrins, which are difficult to crystallize, and by their very nature are designed to react with light and oxygen, use of the NSLS has greatly enhanced our ability to obtain high quality molecular structures on these marginally stable compounds. In comparison to a conventional diffractometer, we get faster data collection on much smaller crystals. We have recently reported the synthesis and structural characterization (A. Phadke *et al.*, in press) for a new benzochlorin photosensitizer 1 from data measured at X7B.

Methods and Materials: Single crystals of 1 were grown from mixtures of methylene chloride and methanol. Two hemispheres of data were collected at 145K by the rotation method using a MAR345 image plate detector. The data were processed and merged with Denzo/Scalepack (Z. Otwinowski and W. Minor, 1997) and the structure was solved and refined with the SHELXTL package (G. Sheldrick, 1995).

Results: The molecular structure of 1 is shown in **Figure 1**.

Conclusions: This determination provides an unambiguous identification of 1 and the first stereochemical parameters for this new class of benzochlorins. The molecular structure will be used as a model for theoretical studies for predicting its properties and for designing more efficient sensitizers for PDT.

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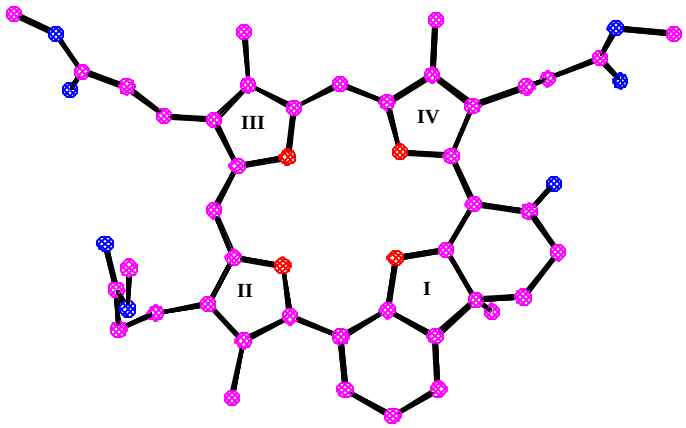

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Figure 1. Structure of 1 showing the porphyrin framework. Ring I is the reduced ring. Hydrogen atoms have been omitted for clarity. The crystal used for the data collection measured 0.225 x 0.088 x 0.025 mm.